more clearly describe the invention. Finally, the limitation of a pH in the skin-physiologically tolerable range was added to claim 27.

Claim 27 is now directed, inter alia, toward a pharmaceutical composition for the treatment of seborrheic dermatitis, wherein said composition is of a pH in the skin-physiologically tolerable range. This limitation is supported in the specification at 8, lines 29 to 30.

New claims 32-37 have been added. Support for these new claims is found in the specification and claims as originally filed.

Claim 34 has been added to claim a pharmaceutical composition comprising a 1-hydroxy-2-pyridone of the formula I and at least one surfactant, and having a pH from about 4.5 to about 6.5. This claim finds support in the claims in the specification at page 2, line 31, at page 8, line 30, and in other places in the application as filed. Claim 34 differs from claim 27 in the definition of the radical R^4 and in the definition of the applicable pH range limitation.

I. Rejection Under 35 U.S.C. § 102(b)

The Examiner rejected pending claims 27 and 29-31 as being anticipated by Dittmar et al. (U.S. 4,185,106). Office Action at 2. Because of the amendments to the claims and the arguments set forth below, this rejection should be withdrawn.

Applicants respectfully contend that Dittmar et al. do not anticipate the claims as amended. Dittmar et al. teach compositions containing certain 1-hydroxy-2-pyridones

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D.C. 20005
202-408-4000

for the treatment of dandruff, but do not teach a composition of a certain pH. Claim 27, as amended, does not read upon the disclosure of Dittmar et al. While Dittmar's substituent R^1 may be phenyl-oxy-alkyl, this does not anticipate the corresponding radical of formula II in present claim 27. The phenyl portion of the radical of formula II must be further substituted with an aryl substituent, and Dittmar's phenyl-oxy-alkyl substituent cannot be. Nor would Dittmar et al. render obvious this radical of formula II. Compare the radical of formula II, shown above in amended claim 27.

Added claim 34 is not anticipated by Dittmar et al. Claim 34 recites a pharmaceutical composition for treating seborrheic dermatitis, comprising a 1-hydroxy-2-pyridone and at least one surfactant, having a pH from about 4.5 to about 6.5. At col. 9, lines 22-28, Dittmar et al. state: "In all the compositions on the basis of the mentioned complex compounds with organic amines, the pH-value has always to exceed 7.5, generally even 8.8, to prevent precipitation. For this reason, it has not been possible to produce weakly acidic compositions . . . which would comply with the pH-value of the skin and hair." And again, at lines 40-41: "the compounds used according to the invention do, however, not have these considerable disadvantages." This language does not teach a composition having a pH of 4.5 to 6.5. At most, Dittmar et al. teach a composition having a pH below 7.5. This reference therefore does not anticipate claim 34 nor any claim of the present application.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D. C. 20005
202-408-4000

II. Rejection of Claims Under 35 U.S.C. § 103(a)

A. Claims 27 and 29-31 were rejected as being unpatentable over Dittmar et al. (U.S. 4,185,106) in view of Lohaus et al. (U.S. 4,797,409). Office Action at 3. Applicants respectfully disagree, and explain why this rejection should now be withdrawn.

The present invention relates to, among other things, compositions comprising certain 1-hydroxy-2-pyridones with at least one surfactant, and having a particular pH, for the treatment of seborrheic dermatitis. *See* Specification at 1. Quite surprisingly and unexpectedly, the compositions of the present invention act as both antiinflammatory agents and antimycotic agents, thus providing a novel, efficacious, and comprehensive treatment for this disease. *Id.* Significantly, seborrheic dermatitis differs from simple dandruff "by the presence of erythema as a sign of inflammation, by the greater degree of scaling with occasional itching and burning, and by the occurrence of eczematous changes to other body sites." *Id.* at lines 4-7. Thus, at a minimum, references teaching only antidandruff or antimycotic properties of related 1-hydroxy-2-pyridones would not render obvious the present invention.

Dittmar et al. teach away from the use of 1-hydroxy-2-pyridones for the treatment of seborrheic dermatitis. Dittmar's compositions may further "contain . . . antiseborrheic agents" in addition to 1-hydroxy-2-pyridones. Col. 6, line 24. This statement would discourage a skilled practitioner of the art from pursuing Dittmar's compounds as antiseborrheic agents.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D.C. 20005
202-408-4000

The compositions of the present invention are not obvious in light of Dittmar's compositions. Claim 34 of the present application recites a pharmaceutical composition comprising an efficacious amount, for the treatment of seborrheic dermatitis, of a 1-hydroxy-2-pyridone and at least one surfactant, having a pH of about 4.5 to 6.5. These elements are not taught nor suggested by Dittmar et al, either alone or in combination with any other reference. For example, Dittmar et al. exemplifies 1-hydroxy-4-methyl-6-cyclohexyl-2-pyridone (col. 2, line 56), which appears in present claim 37. However, nothing in Dittmar et al. teaches this compound in a composition, in an efficacious amount for the treatment of seborrheic dermatitis with a surfactant at a pH of about 4.5 to about 6.5. Dittmar et al., as mentioned above, teaches away from treatment of seborrheic dermatitis with these compounds. Col. 6, line 24. Teachings of the proper pH for such treatment also do not appear. Taken as a whole, this reference does not suggest the desirability of making the present invention.

Nothing disclosed by Lohaus et al. changes this. Lohaus et al. teach 1-hydroxy-2-pyridones which have antimycotic, antibacterial, and antiviral activities. However, this reference does not teach, nor make obvious, the present invention. Lohaus et al. determine antimycotic behavior against the "skin fungus" Trichophyton mentagrophytes in col. 13, line 22. No connection is made to seborrheic dermatitis, and the disclosure does not even mention seborrheic dermatitis. On page 1 of the specification for the present application, yeast fungi of the strain Pityrosporum are

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D. C. 20005
202-408-4000

"assumed to be the cause of seborrheic dermatitis." Specification at page 1, line 33. Pityrosporum yeast fungi are not mentioned by Lohaus et al.

Combining Lohaus et al with Dittmar et al. does not offer a reasonable expectation of success, because Dittmar et al. clearly state that disclosed compositions may further comprise antiseborrheic agents, and Lohaus et al. do not identify any 1-hydroxy-2-pyridone compounds as antiseborrheic agents.

B. The Examiner rejected claims 14-26 as being unpatentable over Lohaus et al. (U.S. 4,797,409) and Dittmar et al. (U.S. 4,185,196) in view of Yoshimasa et al. (J. SCCJ, 22(3), 165-70, (1988); CAPlus abstract). Office Action at 4. In the same section of the Office Action, mention is made of Saint-Leger et al. (J. Soc. Cosmet. Chem., 40(2), 109-118, (1989); Biosis abstract). Office Action at 5. Applicants respectfully disagree.

Lohaus et al. teaches 1-hydroxy-2-pyridones of the formula I as effective antimycotics, antibiotics, and antiviral agents. Specifically, the disclosed compounds were tested against Trichophyton mentagrophytes, a skin fungus. See col. 13, line 22. Lohaus et al. provides no connection between this skin fungus and seborrheic dermatitis. In fact, Lohaus et al. never mentions seborrheic dermatitis. Moreover, Lohaus et al. do not teach nor suggest the proper pH range at which medicaments comprising disclosed compounds would work for any purpose, nor whether compositions thereof could contain surfactants.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D. C. 20005
202-408-4000

Dittmar et al. teach away from the use of 1-hydroxy-2-pyridones as antiseborrheic agents. *See* Dittmar et al. at col. 6, line 24. Nothing in Lohaus et al. reverses this teaching of Dittmar et al.

The Examiner alleged that the present invention is rendered obvious by Lohaus et al. and Dittmar et al. in light of Yoshimasa et al. and Saint-Leger et al. Office Action at 5. Yoshimasa et al. teach that Pityrosporum ovale (P. ovale) is a yeast "closely related to seborrheic dermatitis." These researchers tested, inter alia, the effect of three "antidandruff agents" as inhibition agents of P. Ovale. These three were hinokitiol, zinc pyrithione, and a 1-hydroxy-2-pyridone, piroctone olamine. Teaching away from the present invention, Yoshimasa et al. clearly state: "Hinokitiol was the most effective inhibitor of P. ovale." Thus, Yoshimasa et al. characterize a 1-hydroxy-2-pyridone as an antidandruff agent and find that hinokitiol is the more effective inhibitor of P. ovale.

Hinokitiol (β-thujaplicin) is not a 1-hydroxy-2-pyridone, yet its structure resembles that of a 1-hydroxy-2-pyridone. See Aldrich Chemical Catalogue, p. 1607 (1998) (a copy thereof is attached). Specifically, an hydroxyl group is alpha to a carbonyl. Reading Yoshimasa et al., one skilled in the art would recognize the remote similarities of these structures and would pursue antimycotic applications with hinokitiol instead of 1-hydroxy-2-pyridones of the present invention.

Saint-Leger et al., hypothesizing that P. ovale is a cause of dandruff, compare the activities of two antifungal shampoos against dandruff. They find that Octopirox (a

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N.W.
WASHINGTON, D.C. 20005
202-408-4000

1-hydroxy-2-pyridone) reduces scaling and P. ovale more effectively than magnesium omadine. Yet no connection appears between P. ovale and seborrheic dermatitis. Only when Saint-Leger et al. is viewed in light of Yoshimasa et al. does a connection appear. However, this connection would cause a skilled practitioner to favor hinokitiol over a 1-hydroxy-2-pyridone. Saint-Leger et al. do not overcome this preference. Moreover, reading these two documents in light of Dittmar et al. and Lohaus et al. does not change anything. These documents do not combine to motivate one skilled in the art to try the compositions of the present invention.

C. Claim 28 was rejected as being unpatentable over Lohaus et al. (U.S. 4,797,409) and Dittmar et al. (U.S. 4,185,196) in view of Kamegai et al. (U.S. 5,753,600). Office Action at 6. Applicants respectfully disagree.

Lohaus et al. teaches the antimycotic properties of 1-hydroxy-2-pyridones against Trichophyton mentagrophytes. No mention of seborrheic dermatitis nor of any microbes related to seborrheic dermatitis is made. Dittmar et al. teach antidandruff properties of certain 1-hydroxy-2-pyridones, and teach away from their use as anti-seborrheic agents. See Dittmar et al. at col. 6, line 24. Kamegai et al. teach antibacterial detergent compositions comprising saccharide nonionic surfactants, antibacterial agents, and other surfactants. Kamegai's compositions may comprise salts of certain 1-hydroxy-2-pyridones, and may have a pH adjusted to 2-10, preferably 4-8. See col. 6, lines 39-41.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N.W.
WASHINGTON, D.C. 20005
202-408-4000

Kamegai et al. fails to teach or suggest at what pH the disclosed 1-hydroxy-2-pyridones might have an effect on seborrheic dermatitis. Indeed, Kamegai et al. fail to mention that these compounds even have antimycotic activity. No motivation exists to combine the 1-hydroxy-2-pyridones of Lohaus et al. with the surfactants mentioned by Dittmar et al. at the pH given by Kamegai et al. to treat seborrheic dermatitis. Only improper hindsight provided by the benefit of the present invention provides such motivation.

III. Conclusion

Dittmar et al. specifically teach against using compounds related to the inventive compounds for treating seborrheic dermatitis. Lohaus et al. do not teach antiseborrheic activity, nor activity against any yeast associated with seborrheic dermatitis. Yoshimasa et al. teach hinokitiol to be the better inhibitor of P. ovale than a 1-hydroxy-2-pyridone. Saint-Leger et al. teach a 1-hydroxy-2-pyridone, characterized as an antidandruff agent, as having an affect on P. ovale, yet do not overcome the preference established by Yoshimasa et al. Kamegai et al. teach salts of certain other 1-hydroxy-2-pyridones in detergent compositions in broad pH ranges, but do not suggest antimycotic properties of these salts. Taking each reference as a whole, while ignoring the unexpected and surprising teachings of the present application, there exists no motivation to combine selected elements of these references. Nor is there a

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D.C. 20005
202-408-4000

reasonable expectation of success found in that selective and unintuitive combination without the hindsight afforded by the present invention.

Applicants therefore respectfully request that the above Amendment be entered, and the claims as amended be reconsidered in light of the arguments set forth above.

If there is any fee due in connection with the filing of this Statement, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: _____
Allen R. Jensen
Reg. No. 28,224

Dated: September 21, 1999

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N.W.
WASHINGTON, D.C. 20005
202-408-4000